The Frequency of Asymptomatic Disturbances of Cardiac Rhythm and Conduction in Middle-Aged Men*

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A study of a random sample of 301 actively employed American men, of median age 55 years, employing cardiac recordings obtained during six-hour periods of ordinary activity indicates that asymptomatic periods of dysrhythmia and conduction disturbances occurred in 92.6 per cent of these men at some time during the recording period.

Supraventricular premature contractions and other supraventricular dysrhythmias were found in 76.0 per cent of the recordings. These were not associated with present evidence of coronary heart disease or with subsequent death from coronary heart disease, except when supraventricular dysrhythmias were associated with other dysrhythmias or conduction defects.

Ventricular premature contractions and complex ventricular dysrhythmias were found in 62.2 per cent of the recordings. These were significantly associated with the presence of coronary heart disease at the time of the examination. They were also associated with an enhanced risk of subsequent death from coronary heart disease.

Defects of cardiac conduction, constant or transient, were found in 6.7 per cent of the men. These, too, were associated with an enhanced risk of subsequent death from coronary heart disease.

FOR MANY YEARS it has been known that unexpected and apparently asymptomatic disorders of cardiac rhythm and conduction may be discovered during the examination of apparently healthy people. During the last decade, as it has become customary to monitor the electrocardiograms of patients during episodes of acute coronary heart disease, it has become evident that asymptomatic disturbances of rhythm and conduction are exceedingly frequent at such times; and it has been recognized that a large proportion of deaths that occur in hospitals after acute myocardial infarction are the result of the sudden occurrence of cardiac standstill or of dysrhythmias.[1] It is also recognized that a large proportion of the deaths that take place outside the hospital and are apparently caused by coronary heart disease occur quite suddenly. Many people who die in this manner are found at autopsy to show evidence of coronary atherosclerosis but no evidence of a recent acute coronary occlusion or myocardial infarct.[2,3] The inference has been that these people also die from cardiac standstill or acute dysrhythmias.

These observations raise the question of how frequently asymptomatic disturbances of rhythm and conduction may occur in apparently healthy people during the course of their ordinary activities and whether their occurrence may be associated with an increased risk of death from coronary heart disease. The development of recording devices that make it possible to obtain continuous records of the electrocardiograms of active people over long periods of time has made it possible to investigate this question.[4] This paper describes an effort to determine the frequency with which asymptomatic disturbances of rhythm and conduction occurred in a random sample of actively employed middle-aged American men during a six-hour period of ordinary activity, and the relation of these disturbances to subsequent death from coronary heart disease.

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METHODS

SELECTION OF THE SAMPLE

Because coronary heart disease and sudden death are more prevalent in men than in women before the age of 60, the study sample was limited to men of median age 55 years. An industrial population was selected for sampling because of the relative ease with which the characteristics of the men in such populations can be defined, and the relative ease with which the relation of the sample to the population can be determined.[5] Within such a population there is also a relatively unequivocal definition of the term "actively employed."

The sample was obtained from an age cohort of men whose 30 year experience with coronary heart disease had first been investigated.[6] The cohort was selected by obtaining a complete list of all men who were on the payroll of the New Jersey Bell Telephone Company on January 1, 1935. From this list all men were designated who had been born between January 1, 1902, and December 31, 1908, and who had been hired between January 1, 1923, and December 31, 1930. Eleven hundred and sixty men, of median age 30 years in 1935, were designated by this procedure. The 30 year experience of these men was traced by various means, and the status of all but 8 members of the cohort on January 1, 1962, was ascertained. It was determined that there had been 65 deaths from coronary heart disease, yielding a rate of 5.64/100 during the intervening years. This rate is very close to the national death rates for white men during this period.[6]

On November 1, 1962, 856 men from this cohort were still on the active payroll of the company. These men were defined as "actively employed." From this group a random sample was drawn. This was stratified according to the organizational level of the men and the level of their education at the time that they were hired, because both of these variables have been shown to be associated with differences in the risk of coronary heart disease in this population.[7] The sample, as drawn, consisted of 103 workmen, 57 foremen, 101 supervisors and 95 managers and executives (total 356). All of the workmen and foremen, 50 of the supervisors, and 44 of the managers and executives had had no college degrees when hired and were classified in a "no-college group." Fifty-one supervisors and 51 executives were men of college background. The slight inequalities between the numbers of men from the two backgrounds at supervisory and managerial levels occurred because there were not quite enough supervisors and managers without college degrees on the payroll to fill these two categories completely. Of the 356 men designated, 301 men agreed to participate and were examined completely. These included 79 workmen, 46 foremen, 42 supervisors and 41 managers and executives of "no-college" background, and 44 supervisors and 49 managers and executives of "college" background. Many of the men who would not participate completely nevertheless provided information about themselves or participated in part of the examination. A study of the data from company records and from other sources of information about the 55 men who were not examined completely indicated that their rates for coronary heart disease and for subsequent coronary deaths were not significantly different from the rates among the 301 men who were examined completely. The evidence suggests that little bias has been introduced by our inability to examine completely 15.4 per cent of the men in the sample.[6]

EXAMINATION OF THE MEN IN THE SAMPLE

The medical examinations of the men in this sample were carried out by examiners who had been instructed previously in the uniform system of procedures and coding of data which was used throughout these studies. The medical history was obtained with the aid of a pre-tested medical history questionnaire that participants filled out. This form provided a systematic review of the past medical history and the present symptoms of disease, giving specific attention to the symptoms and signs of cardiovascular disease. It was accompanied by a questionnaire which asked for detailed information about the daily round of activities of the subject on week days and weekends, and during various seasons of the year; his smoking habits; his alcoholic intake; his medications and diet; and the history of illnesses in his family which might be pertinent to coronary heart disease. When the subject had completed this questionnaire, the examining physician reviewed it in detail with him. The examiner then made a graded evaluation of some of the features of the cardiovascular history of the subject, and especially of his history of previous myocardial infarction, coronary insufficiency, and angina pectoris, following the criteria recommended by the Conference on Epidemiology of Cardiovascular Disease Methodology (The "Princeton Conference"),[8] and entered his judgment in a coding form.

The physical examination followed a pre-tested physical examination form. All items were completed by the examiners. Particular attention was paid to phenomena which had been thought to be relevant to coronary heart disease, including some of secondary interest, such as the presence or absence of tophi, xanthelasma, arcus senilis, eyeground changes (graded according to the Keith-Wagoner scale for arteriosclerosis) and the pulses in the peripheral vessels. The blood pressure was taken twice in each arm, at the beginning and end of the examination, with the subject in the sitting position, using a 12 cm. cuff and a mercury manometer. The diastolic level was recorded both when the sound changed and when the sound ended. The cardiovascular examination followed a general form like that originally used in the Framingham survey.[9] Cardiac murmurs, when detected, were described and graded by two observers.

The laboratory diagnostic procedures began with a 6 ft.

posteroanterior roentgenogram of the chest, which was read independently by two roentgenologists, using a standard reporting form. The data from the roentgenogram included measurements of the cardiothoracic ratio, estimates of the degree of calcification and tortuosity of the aorta, and of chamber enlargement of the heart. A standard 12 lead electrocardiogram was obtained in the morning, using a Sanborn Model Viso 100 Direct Writing electrocardiograph, with the subject supine in a rested, fasted state, without having smoked for 8 hours. The electrocardiogram was read independently by two electrocardiographers who had no knowledge of the clinical findings. In the case of conflict in the readings or measurements, a reading from a third cardiologist was obtained. Measurements and manifestations were coded according to the manner suggested by Blackburn et al.,[10] using a standard coding form. Fasting samples of venous blood were examined for ABO blood groups, hematocrit, red blood cell count, white blood cell count and differential, and serologic tests for syphilis were carried out. Serum samples were examined for cholesterol (method of Abell et al.[11]), triglycerides (method of Van Handel and Zilversmit[12]), nonesterified fatty acids (method of Dole[13]), and uric acid concentration (method of Dubbs et al.[14]). In addition to a fasting urine specimen, a second urine specimen was obtained later in the day, two hours after a high carbohydrate meal which included 12 oz. of a sweetened carbonated drink. In the follow-up study a 1 hour glucose tolerance test was carried out according to the method of Hayner et al.,[15] and audiograms were obtained with the use of a Rudmose Automatic Audiometer.

If the history, the examination, or any of the laboratory procedures yielded evidence of a medical condition thought to be relevant to this study, an attempt was made to obtain records and other pertinent data from hospitals, private physicians and the company's medical department. Sometimes other diagnostic procedures were carried out by arrangement.

PROCEDURES FOR CARDIAC RECORDINGS

The initial cardiac recordings were obtained with four Model 350A and four Model 350C Holter Avionics "electrocardiocorders"—small, battery-powered tape recorders that can be worn by the subject and that provide a continuous recording of the electrocardiogram under most conditions of ordinary activity during periods up to 10 hours.[4] In the preparation of the data for analysis, the recordings were processed by means of an "electrocardioscanner," Model 450B, and an "electrocardiocharter," Model 550A. Before use, these instruments were tested for speed constancy, for rate linearity and for timing error. The frequency response of the recorder-scanner and recorder-charter systems, and the effect of the electronic characteristics of the system on the electrocardiographic signal were ascertained.[16]

The recordings were obtained in the following manner: On the night before the recording, the subjects came in pairs to the medical center, and retired before 11 P.M. in rooms provided by us. After at least 8 hours of sleep, they were awakened and taken to the laboratory in a fasting state, without having smoked. Initial blood and urine samples and standard electrocardiograms were obtained. The recorders were then attached, with the electrodes placed over the fifth rib in the nipple line bilaterally. As the recording was started, a Heuer 12 hour chronometer was started also. Throughout the entire recording procedure, the subject was accompanied by a technician, who observed all of the activities of the subject and who timed the beginning and end of each of the routines of activity with the chronometer. At appropriate intervals the technician inserted signals into the recording tape by briefly reversing the polarity of the electrocardiographic signal.

During the course of the day each man followed the same routine. First he spent two minutes in the supine, left lateral, right lateral, standing, sitting and knee-chest positions. Next he performed a Valsalva maneuver. He then performed a standard two-step test according to the specifications of Master.[17] Next he consumed a "breakfast" consisting of 500 cc. of ice water, which was drunk rapidly, and followed, after an interval of several minutes, by the consumption of 500 cc. of hot coffee. This usually was accompanied by the eating of two pieces of toast. Some 10 minutes after the "breakfast" ended, the subject walked out of doors 175 meters to a nearby office. During the next hour he sat at a table, performing standard paper and pencil psychologic tests. According to the estimates of the psychologist, these tests produced moderate anxiety in some men. After a brief interval, he underwent one hour of interview with a sociologist. This interview also aroused moderate anxiety in some men. At the end of the sociologic interview a second blood sample and a urine sample were obtained from him. The subject then walked, out of doors, 125 meters to a cafeteria, where he consumed a meal consisting of an appetizer, soup, meat, vegetables, potatoes, a dessert (pie or ice-cream), and 360 cc. of a sweetened carbonated beverage. Immediately after the meal, he walked up a flight of 13 stairs and 125 meters out of doors, returning to the office. There he again sat at a table performing psychologic tests, or filling out questionnaires, for about two hours, at which point the recorder was removed. The procedure began between 8:30 and 9 A.M. and lasted until 3 to 3:30 P.M. If the subject wished to smoke during the period of the recording he was allowed to do so. A third urine specimen was obtained two hours after the meal. Defecation, if necessary, was allowed during the period of the recording. At the end of the recording most subjects described themselves as "tired."

ANALYSIS OF DATA FROM CARDIAC RECORDINGS[16]

The analog data from the magnetic tapes were fed into the "electrocardioscanner," which generates saw-tooth voltages, the heights of which are propor-

Table I. Recordings Obtained

	No.	% of Total
Men examined	301	100
Recordings obtained	296	98.3
Complete recordings	283	94.0
Complete recordings, accurately timed	264	87.7
Duration of complete recordings (min.)*	367.6 ± 2.62†	
No. of complexes/complete recording	30,272 ± 644.8†	

* Based on 264 accurately timed recordings.
† Two times standard error of the mean.

tional to the R–R intervals. These voltages, in turn, were fed into a multitrace oscilloscope photographic recorder, Model DR8 Rapid Writer (Electronics for Medicine Corporation), where they were displayed on a cathode ray tube with an independent time base, and calibrated against 60 c.p.s. current. This so-called arrhythmiagraph trace was then photographed in its entirety, with 1 minute time lines superimposed. Each period of activity was located precisely on the record by comparing these time lines with landmarks in the record which were created by changes of position or activity, and with the polarity signals that were inserted into the record by the technician. These, in turn, were related to the actual elapsed recording time as measured by the chronometer. Heart rates were measured directly from the photographic record with a calibrated platen. By making an appropriate adjustment based on the cumulative timing error of the tape, mean heart rates were calculated for each period of the recording, and rates were obtained before, during and after various exercise periods.

For scanning purposes the electrocardiographic complexes themselves might be displayed on a cathode ray tube. The time base of this tube is the saw-tooth voltage initiated by the R wave of each complex, which allowed each complex to be superimposed on the complex preceding it. On this tube the complexes could be scanned at 60 times recording speed ("60 times real time"). For the purpose of direct study the complexes were displayed on another cathode ray tube where they could be scanned in series at recording speed ("real time"), and written out photographically. A series of 20 or more complexes were written out photographically in this manner, with the subject in each of the routine positions, and before, during and after each of the routine activities. The entire record was scanned visually at 60 times recording speed before the photographic analysis, and any significant change in the form of the complex that was observed on this scanning was scanned at recording speed and also was written out photographically.

From the arrhythmiagraph trace it was possible to locate all potential periods of dysrhythmia. If there were fewer than 50 of these, each was scanned at real time, and an example of each type of dysrhythmia or conduction disturbance encountered was written out for direct study. If the number of possible periods of dysrhythmia in a record was greater than 50, a random sample of 10 minutes from each hour was drawn, and each of these minutes was scanned completely at real time, with the number and type of premature complexes and other dysrhythmias and conduction disturbances carefully counted. The total number of such disturbances in the record was estimated from the real time write-out of this random sample.

The analysis of the taped data from the cardiac recording was carried out by observers who had no knowledge of the medical data relating to the men whose tapes were being examined.

SUBSEQUENT FOLLOW-UP OF THE MEN IN THE SAMPLE

The initial examination of these men was carried out in 1963 and 1964, when the median age of the men in the sample was 58 years. With the agreement of the men, arrangements were made to follow each man's course thereafter. Every episode of absence due to sickness was reported to us, along with all other evidence of illness which the company learned about from its own examinations or from physicians' reports. The men, when queried, provided additional data. Whenever there was a death or a sickness-absence that might represent an episode of coronary heart disease, detailed information was obtained from physicians and hospitals, death certificates were obtained, and autopsy reports were sought when available. When possible, details about the circumstances of deaths were obtained from family members or from friends and associates. In 1967, we began to re-examine these men, using procedures identical to those previously described. On this occasion a second 24 hour monitoring of their electrocardiograms was carried out. At the time of this writing, 32 deaths have occurred among the 301 original subjects, and 153 men have been re-examined. This report is concerned only with the results of the first examinations and with the deaths; the results of the re-examinations will be reported later.

Results

RECORDINGS OBTAINED

Two hundred and ninety-six recordings were obtained from the 301 men (Table 1). Thirteen of these were incomplete or defective and could not be used for many purposes, although they yielded some usable data. There were 283 complete records which were useful for most purposes, but some of them had minor ambiguities of timing which could not be corrected. Two hundred and sixty-four complete and accurately timed records were obtained. The average duration of the 264 accurately timed records was 367.6 ± 2.62 min., or approximately 6 hours. The average number of cardiac complexes per

Table II. Supraventricular Dysrhythmias (Based on 283 Complete Recordings)

	No.	% of Total
Recordings containing 1 or more SPC's	215	76.0
Less than 1/1,000 complexes	179	63.2
1 to 9.999/1,000	18	6.4
10 or more/1,000	18	6.4
Recordings containing one or more complex supraventricular dysrhythmias	50	17.7
Supraventricular bigeminy	11	3.9
Supraventricular trigeminy	9	3.2
Paired SPC's	34	12.0
Multiple consecutive SPC's	13	4.6
Paroxysmal supraventricular tachycardia	2	0.7

SPC = supraventricular premature contraction.

complete record was 30,272 ± 644.8.* The distribution of the complete recordings in relation to the distribution of evidences of coronary heart disease among the men (see later) was not significantly different from that which would be expected if all recordings had been complete. This suggests that no significant bias was introduced by our inability to study the 6 per cent of recordings that were defective.

During the course of the recordings, 5 men complained of pains which lasted for a short time and which had the characteristics of angina pectoris. None of these episodes coincided with a period of dysrhythmia. A few of the men who had many premature contractions in their records admitted, when questioned, to being aware of irregularities of their heartbeat, but none complained of this spontaneously.

DYSRHYTHMIAS OF SUPRAVENTRICULAR ORIGIN

The modified Lewis lead, which was used for the initial series of recordings, did not always provide an image of the P wave which could be distinguished from the low frequency, low voltage noise that often occurs in recordings made from active men. Because of this, one could not always tell whether a premature complex with a regularly conducted QRS had originated in the atrium or in the A–V junction. We have therefore categorized all such dysrhythmias as "supraventricular."

Three-fourths (76.0 per cent) of the 283 complete records contained one or more supraventricular premature contractions (Table II). Eighteen recordings (6.4 per cent) contained more than 10 supraventricular premature contractions/1,000 complexes. Eleven recordings contained bigeminal and 9 trigeminal rhythms of supraventricular origin. Thirty-four recordings (12.0 per cent) contained paired supraventricular premature complexes. Thirteen (4.6 per cent) contained multiple consecutive (three or more consecutive) supraventricular premature complexes, and two recordings (0.7 per cent) contained periods of paroxysmal supraventricular tachycardia. On the standard electrocardiographic write-out multiple consecutive supraventricular premature contractions might easily be mistaken for brief runs of paroxysmal supraventricular tachycardia; but on the arrhythmiagraph tracing (Fig. 1) they could be distinguished readily because of the slight irregularity of the rhythm during periods of multiple consecutive premature contractions.

Figure 2 shows the distribution of recordings according to the number of supraventricular

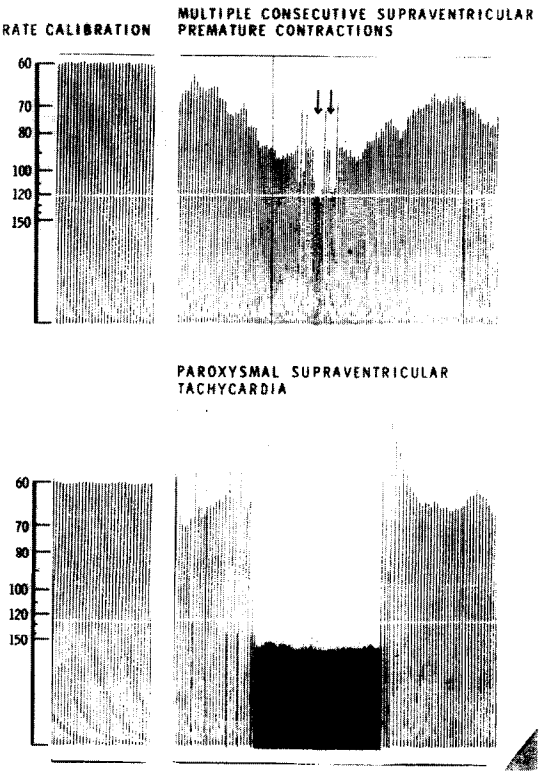

Figure 1. *Arrhythmiagraph tracing.* Contrast between the appearance of episodes of multiple consecutive premature contractions (**top panel**) and paroxysmal supraventricular tachycardia (**bottom panel**). Both episodes are preceded by isolated supraventricular premature contractions (SPC's) followed by pauses.

* Variation is expressed as two times the standard error of the mean.

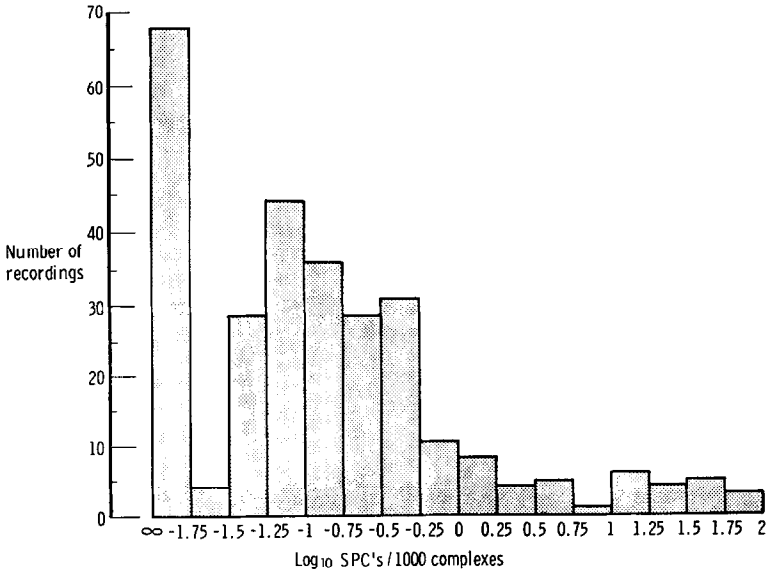

Figure 2. *Distribution of recordings* by number of supraventricular premature contractions in each 1,000 complexes.

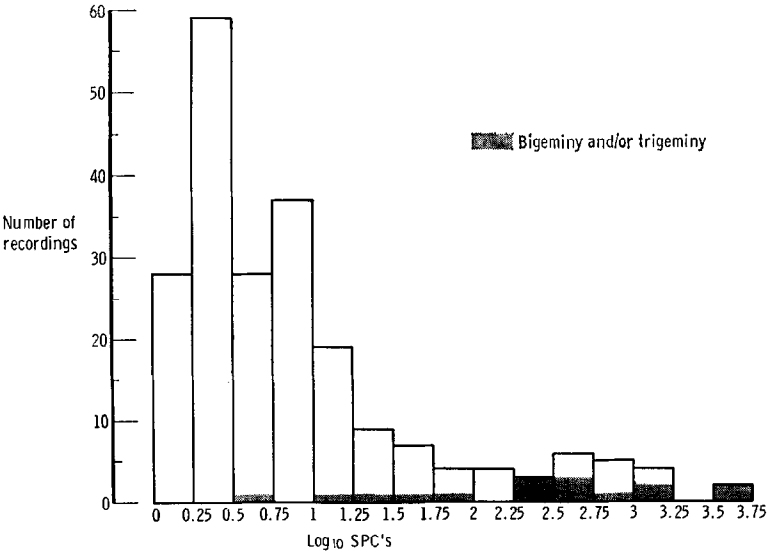

Figure 3. *Relation of recordings containing episodes of supraventricular bigeminy and trigeminy* to distribution of recordings by total number of supraventricular premature contractions (SPC's) in recording.

premature contractions/1,000 complexes. Supraventricular premature contractions ranged from fewer than 1 in 30,000 complexes to almost 1 in every 10 complexes. Because the distribution is so widely dispersed, the abscissa of the histogram has been scaled logarithmically. The distribution is not that which one would expect if supraventricular premature contractions were rare events which sometimes occur in all records and have an equal chance of occurring in any record. It appears to be bimodal, but the mode at less than 10^{-2} supraventricular premature contractions/1,000 complexes might be an artifact resulting from the limited size of the sample (3×10^4 complexes). A sample of say 10^{10} or 10^{20} complexes might have revealed this mode to be a long tail made up of records containing very rare supraventricular premature contractions. The distribution does not "fit" a Poisson distribution. It is better explained by a

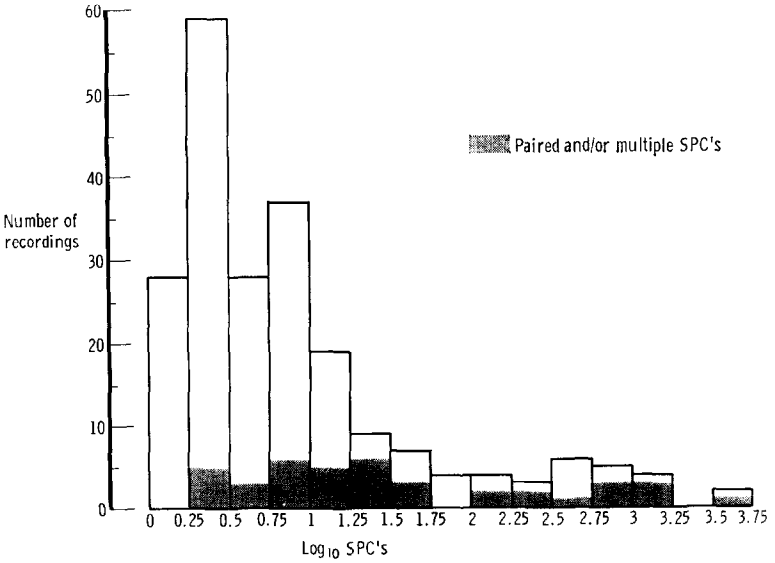

Figure 4. *Relation of recordings containing episodes of paired and multiple consecutive supraventricular premature contractions (SPC's)* to distribution of recordings by total number of such beats in recording.

hypothesis that the men whose records contained many supraventricular premature contractions have some condition or conditions which greatly increased their likelihood of having these dysrhythmias.

COMPLEX SUPRAVENTRICULAR DYSRHYTHMIAS

Complex supraventricular dysrhythmias were found more frequently in records which contained many supraventricular premature contractions (Fig. 3 and 4). However, the frequency of occurrence of supraventricular dysrhythmias such as paired or multiple premature beats does not appear to be a simple linear function of the frequency of supraventricular premature contractions. Apparently, as their frequency increases, the frequency of supraventricular bigeminy and trigeminy increases roughly in parallel. As a result, records in which there are frequent supraventricular premature contractions contain approximately as many episodes of bigeminy and trigeminy as might be expected if the number of supraventricular premature contractions in the record was the sole factor affecting their occurrence (Table III). On the other hand, as the frequency of supraventricular

Table III. Relation Between Complex Supraventricular Dysrhythmias and Frequency of Supraventricular Premature Contractions (SPC's) in Recordings (Based on 215 Recordings Containing SPC's)

Dysrhythmias		Categories of Recordings Based on Frequency of SPC's/1,000 Complexes											
		<1/1000				1.000–9.999/1,000				≥10/1,000			
		Recordings with Dysrhythmias			Ratio of Dysrhythmias to SPC‡	Recordings with Dysrhythmias			Ratio of Dysrhythmias to SPC‡	Recordings with Dysrhythmias			Ratio of Dysrhythmias to SPC‡
Type	Recordings	No.	%*	No. Expected†		No.	%*	No. Expected†		No.	%*	No. Expected†	
1 or more SPC's	215	179	83.2	...	...	18	8.4	...	...	18	8.4	...	...
Supraventricular bigeminy	11	3	27.3	9.16	1/347	2	18.2	0.92	1/96	6	54.5	0.92	1/157
Supraventricular trigeminy	9	0	0	7.50	0/1,041	3	33.3	0.75	1/308	6	66.7	0.75	1/254
Paired SPC's	34	20	58.8	28.30	1/42	7	20.6	2.85	1/103	7	20.6	2.85	1/167
Multiple consecutive SPC's	13	5	38.5	10.82	1/74	3	23.1	1.09	1/220	5	38.5	1.09	1/1,674

* Per cent of row total.

† Number of recordings "expected" is based on the assumption that the proportion of recordings containing a given complex dysrhythmia will be the same in each frequency category as in the whole population.

‡ This ratio is obtained by dividing the total number of instances of a given complex dysrhythmia in all recordings in a given frequency category by the total number of SPC's in all recordings in this category. Paired and multiple consecutive SPC's are significantly less frequent (p 0.005) in relation to SPC's in the records which contain many SPC's.

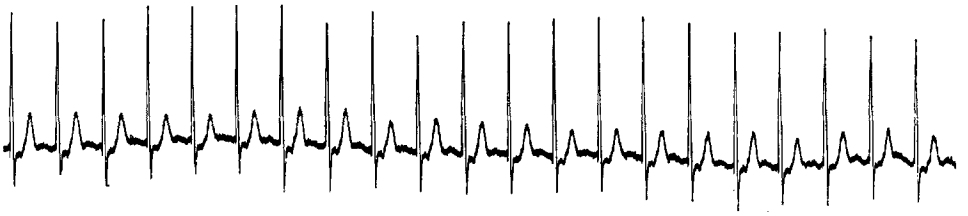

Figure 5. *Photographic write-out of a period of supraventricular (A–V nodal) tachycardia.* Paper speed 25 mm./sec. Ventricular rate 125/min.

premature contractions increases, the relative frequency of paired or multiple consecutive supraventricular premature contractions decreases; although the number of episodes of pairs and of multiple supraventricular premature contractions in records with many supraventricular premature contractions is greater, the number of complex dysrhythmias/supraventricular premature contractions is smaller. Records that contain frequent supraventricular premature contractions do contain more episodes of pairs and multiple supraventricular premature contractions than are found in records that contain few supraventricular premature contractions. However, these records do not have so many episodes of these dysrhythmias as would be expected if the number of supraventricular premature contractions in the record was the sole factor affecting their occurrence. In fact, there were several records in which paired supraventricular premature contractions and multiple consecutive supraventricular premature contractions occurred as almost isolated phenomena.

Table IV. Ventricular Dysrhythmias (Based on 283 Complete Recordings)

	No.	% of Total
Recordings containing 1 or more VPC	176	62.2
Less than 1 VPC/1000 complexes	96	33.9
1 to 9.999 VPC's/1000	55	19.4
10 or more VPC's/1000	25	8.8
Recordings containing one or more complex ventricular dysrhythmias	54	19.1
Ventricular bigeminy	24	8.5
Ventricular trigeminy	17	6.0
Paired VPC's	36	12.7
Paroxysmal ventricular tachycardia	9	3.2
Recordings containing VPC's from 1 to 4 foci		
From 1 focus only	82	29.0
From 2 foci	66	23.3
From 3 foci	23	8.1
From 4 or more foci	5	1.8

VPC = ventricular premature contraction.

The data suggest that these complex supraventricular dysrhythmias are dependent on the presence of mechanisms which are different in the case of bigeminy and trigeminy on the one hand, and in the case of paired and multiple supraventricular premature contractions on the other hand. Such mechanisms may be present in those who have few supraventricular premature contractions. In such men the isolated occurrence of a supraventricular premature contraction may lead to a period of sustained ectopic rhythm of a more complex nature. This is especially true of pairs and multiple supraventricular contractions.

A–V NODAL RHYTHMS

A–V nodal premature contractions and other A–V nodal rhythms were grouped with the supraventricular rhythms for reasons which have been stated. Two men had periods of paroxysmal supraventricular tachycardia which could be identified as originating in the A–V node (Fig. 5).

VENTRICULAR DYSRHYTHMIAS

One hundred and seventy-six of the 283 complete recordings (62.2 per cent) contained one or more ventricular premature contractions (Table IV). Twenty-five records (8.8 per cent of the total) contained 10 or more ventricular premature contractions/1,000 complexes. Another 55 records (19.4 per cent of the total) contained from 1 to 10 ventricular premature contractions/1,000 complexes.

Twenty-four recordings (8.5 per cent of the total) contained periods of ventricular bigeminy; 17 recordings (6.0 per cent) contained periods of ventricular trigeminy; 36 (12.7 per cent) included paired ventricular beats; and 9 contained periods of three or more consecutive ventricular complexes—technically "paroxysmal ventricular tachycardia" (Fig. 6). Ninety-four recordings (33.2 per cent) contained ventricular premature contractions which originated from

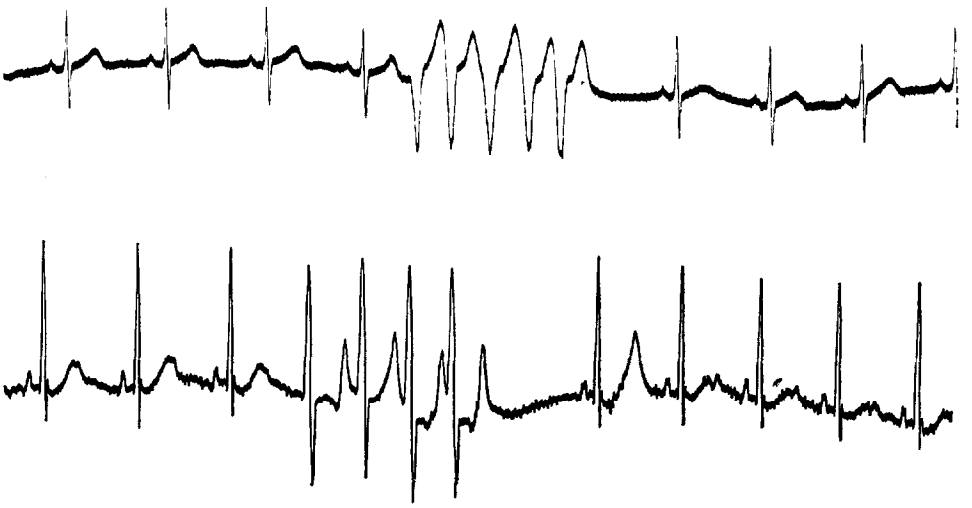

Figure 6. *Photographic write-out of two isolated episodes of paroxysmal ventricular tachycardia.* Paper speed 25 mm./sec.

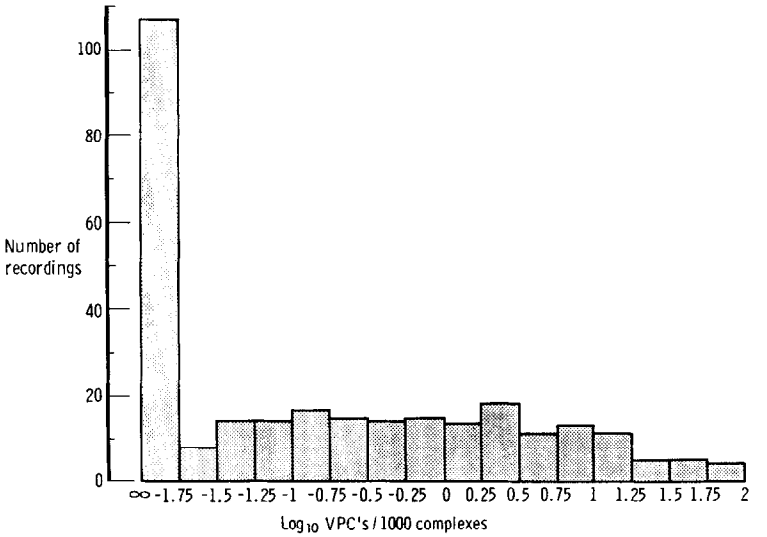

Figure 7. *Distribution of recordings* by number of ventricular premature contractions (VPC's) in each 1,000 complexes.

more than one focus. Five recordings (1.8 per cent) contained ventricular premature contractions that arose from as many as four foci.

VENTRICULAR PREMATURE CONTRACTIONS

Figure 7 shows the distribution of ventricular premature contractions. The range is from less than 1 in 30,000 complexes to almost 1 in 10 complexes. This distribution also is widely dispersed. Its apparent bi-modality may be explained by the same considerations of sample size that applied in the case of supraventricular premature contractions. The distribution will not fit the Poisson assumption of rare events with an equal probability of occurring. It, too, is better explained by a hypothesis that the men with ventricular premature contractions have some condition or conditions which increase the likelihood that such dysrhythmias will occur.

COMPLEX VENTRICULAR DYSRHYTHMIAS

Ventricular bigeminy and trigeminy, paired ventricular beats and paroxysmal ventricular tachycardia were more common in those records that contained many ventricular premature contractions (Figs. 8 and 9). However, the relation between complex ventricular dysrhythmias and ventricular premature contractions is not

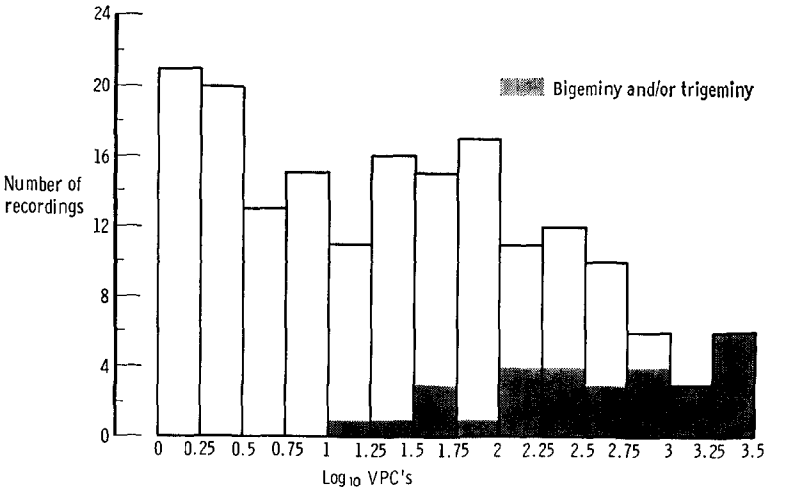

Figure 8. *Relation of recordings containing episodes of ventricular bigeminy and trigeminy* to distribution of recordings by total number of ventricular premature contractions (VPC's) in recording.

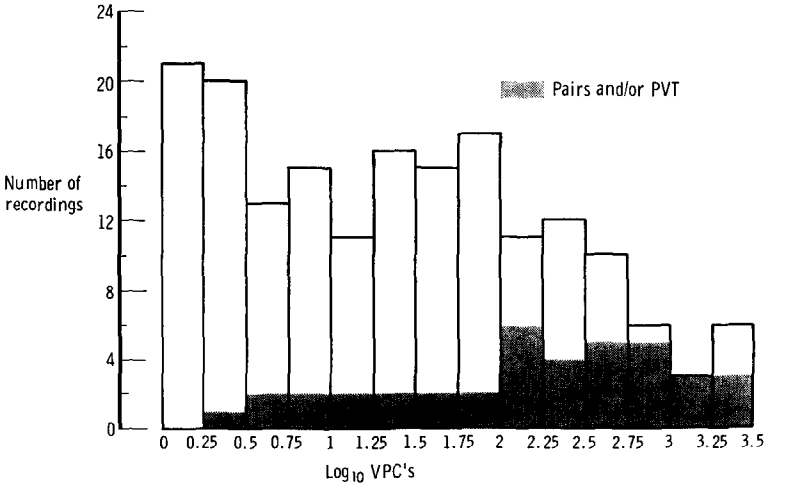

Figure 9. *Relation of recordings containing episodes of paired ventricular premature contractions (VPC's)* and *paroxysmal ventricular tachycardia (PVT)* to distribution of recordings by total number of ventricular premature contractions in recording.

exactly like the relation between complex supraventricular dysrhythmias and supraventricular premature contractions. The number of complex ventricular dysrhythmias is greater in those records with many ventricular premature contractions, but in no case does the number appear to increase directly in parallel with the number of premature contractions in the record. Bigeminy and trigeminy tend to become more frequent as ventricular premature contractions become more frequent (Table v). As a result, records containing many ventricular premature contractions had more than the expected number of episodes of bigeminy and trigeminy. Paired ventricular beats and paroxysmal ventricular tachycardia become relatively less frequent as the number of ventricular premature contractions increases. Although records containing many ventricular premature contractions contain more episodes of pairs and paroxysmal ventricular tachycardia also, the number is not as great as would be expected if the number of episodes of pairs and ventricular tachycardias were a direct function of the number of ventricular premature contractions in the record. Some episodes of ventricular tachycardia and of paired ventricular beats have been found in quite isolated locations in records that contained few other ventricular complexes (Fig. 6). It appears that the occurrence of paired and multi-

Table V. Relation Between Complex Ventricular Dysrhythmias and Frequency of Ventricular Premature Contractions (VPC's) in Recordings (Based on 176 Recordings Containing VPC's)

Dysrhythmias		Categories of Recordings Based on Frequency of VPC's/1,000 Complexes											
		<1/1,000				1.000–9.999/1,000				≥10/1,000			
		Recordings with Dysrhythmias			Ratio of Dysrhythmias to VPC	Recordings with Dysrhythmias			Ratio of Dysrhythmias to VPC	Recordings with Dysrhythmias			Ratio of Dysrhythmias to VPC
Type	Total Recordings	No.	%*	No. Expected†		No.	%*	No. Expected†		No.	%*	No. Expected†	
1 or more VPC's	176	96	54.5			55	31.3			25	14.2		
Ventricular bigeminy	24	1	4.2	13.09	1/770	8	33.3	7.50	1/224	15	62.5	3.41	1/66
Ventricular trigeminy	17	1	5.9	9.27	1/770	5	29.4	5.31	1/570	11	64.7	2.42	1/153
Paired VPC's	36	6	16.7	19.64	1/128	14	38.9	11.25	1/123	16	44.4	5.11	1/85
Paroxysmal ventricular tachycardia	9	2	22.2	4.91	1/385	4	44.5	2.81	1/1,046	3	33.3	1.28	1/3,106

* Per cent of row total.
† Based on per cent of all recordings in this category.
Number of recordings "expected" was obtained by the same procedure as that used in Table III. Ventricular bigeminy and trigeminy occur more frequently (p 0.005) in relation to VPC's in records containing many VPC's; paired VPC's and paroxysmal ventricular tachycardia occur less frequently (p 0.05 and 0.005, respectively).

ple ventricular premature contractions is related to a mechanism that is not simply dependent upon the frequency of premature contractions. In hearts in which such mechanisms are present the occurrence of an isolated ventricular beat may be followed by a series of such beats of variable duration.

DISTURBANCES OF CONDUCTION

Twenty-four records contained evidence of transient or constant disorders of conduction (Table VI). There were 2 instances of atrioventricular block of second degree or higher, and 4 instances of prolonged sinus pauses that may have represented periods of sinoatrial block. There were 2 records with left bundle branch block and 6 with right bundle branch block, including 1 in which right and left bundle branch block alternated. The Wolff-Parkinson-White phenomenon (the pre-excitation syndrome) was found in 2 records. There were 5 other records with constant intraventricular block characterized by a QRS time of greater than 0.10 sec. In 2 of these records the form of the block shifted in its characteristics. There were also 5 records which demonstrated transient and sometimes isolated complexes that were characterized by a QRS time greater than 0.10 sec. When these "transient intraventricular blocks" occurred in subjects whose records also contained many ventricular premature complexes, the pathway of QRS conduction was often quite similar to the pathway of many of the ventricular ectopic beats. Twenty-three other records contained isolated complexes in which the QRS time appeared to be prolonged 0.01 or 0.02 sec. beyond the duration of most complexes in the record but did not exceed a duration of 0.10 sec. These complexes were considered to represent possible transient disturbances of intraventricular conduction (Fig. 10).

Table VI. Conduction Defects (Based on 283 Recordings)*

	No. of Instances	%
Sinoatrial block	4	1.4
Atrioventricular block	2	0.7
Intraventricular block	20	7.7
Left bundle branch block	2	0.7
Right bundle branch block	6	2.1
Wolff-Parkinson-White syndrome	2	0.7
Other constant intraventricular blocks	5	1.8
Unchanging configuration	3	1.1
Shifting configuration	2	0.7
Transient intraventricular blocks	5	1.8

* The total number of men who exhibited definite conduction defects was 24; 1 man had alternating right and left bundle branch block and periods of 2:1 atrioventricular block. There were also 23 men who exhibited possible transient intraventricular conduction defects, 2 of whom also had periods of sinoatrial block.

RELATION BETWEEN DYSRHYTHMIAS AND CONDUCTION DEFECTS

Of the 283 complete records, only 22 contained no recognizable period of dysrhythmia and no evidence of an abnormality of intracardiac conduction.

In 66 records the only abnormality of rhythm and conduction consisted of supraventricular premature complexes. Fifty-nine of these contained fewer than 1 supraventricular premature contraction/1,000 complexes. There were 21 rec-

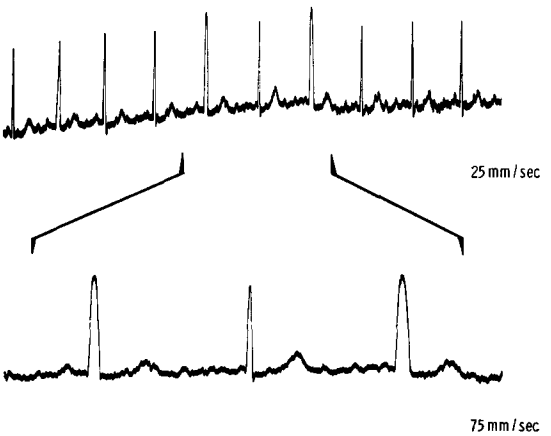

Figure 10. *Example of the transient slight widening of the QRS complex* which has been categorized as "possible transient intraventricular conduction defect." In the **top panel** the paper speed is 25 mm./sec. In the **bottom panel** the paper speed has been increased to 75 mm./sec. to show the change in the three center complexes.

cords in which the only apparent abnormality consisted of ventricular premature complexes; 16 of these contained fewer than 1 ventricular premature contraction/1,000 complexes. In 4 records the only abnormality was an intraventricular conduction defect.

The relation between supraventricular and ventricular premature complexes was studied by means of the rank-order correlation. This yielded a Spearman's rho of 0.122, with a probability of 0.05. Most of this weak association seems to have occurred in men who had many supraventricular or ventricular premature contractions. Such people appear to have been more likely to have premature contractions that originated in other parts of the heart.

The relation between dysrhythmias and conduction disturbances was examined by the chi square technic. Intraventricular blocks of all types were found to be more frequent than expected in subjects who had no supraventricular premature contractions in their records (Table VII). By contrast, they were found to be more frequent than expected in subjects who had a great many ventricular premature contractions (more than 10/1,000 complexes) in their records (Table VIII).

One hundred and forty-five of the records exhibited combinations of supraventricular dysrhythmias, ventricular dysrhythmias and conduction defects, and 20 recordings included one or more examples of supraventricular or ventricular dysrhythmias and also demonstrated conduction defects.

PREVALENCE OF OVERT CORONARY HEART DISEASE AT THE TIME OF THE ORIGINAL EXAMINATION

At the time of the original examination 10 of the 301 subjects met the criteria for having "previous myocardial infarctions" as defined by the Princeton Conference. There were 29 others who met the criteria for other forms of "definite coronary heart disease," such as probable myocardial infarction, acute coronary insufficiency, definite angina pectoris, or electrocardiographic evidence of previous myocardial in-

Table VII. Relation Between Supraventricular Premature Contractions (SPC's) and Conduction Defects (Based on 283 Complete Recordings)

Conduction Defect	Total Instances	Categories of Recordings, Based on Frequency of SPC's/1,000 Complexes									
		0		0.01–0.09		0.1–0.99		1–9.9		>10	
		Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
Sinoatrial block	4	1		2		1					
Atrioventricular block	2	1		1							
Intraventricular block*	20	11	4.86	2	5.35	4	7.25	0	1.27	3	1.27
Right bundle branch block	6	4		1		1					
Left bundle branch block	2	1								1	
Wolff-Parkinson-White	2	1				1					
Other constant intraventricular blocks	5	4								1	
Unchanging configuration	3	2								1	
Shifting configuration	2	2									
Transient intraventricular blocks	5	1		1		2				1	

* Intraventricular blocks of all types are distributed unevenly among the recordings (χ^2 14.94; p 0.005), occurring more often than expected in those containing no SPC's.

Exp. = expected; Obs. = observed.

Table VIII. Relation Between Ventricular Premature Contractions (VPC's) and Conduction Defects (Based on 283 Complete Recordings)

Conduction Defect	Total Instances	Categories of Recordings, Based on Frequency of VPC's/1,000 Complexes									
		0		0.01–0.09		0.1–0.99		1–9.9		>10	
		Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
Sinoatrial block	4	2		1		1					
Atrioventricular block	2	1						1			
Intraventricular block*	20	5	7.53	1	2.54	5	4.30	4	3.87	5	1.76
Right bundle branch block	6	2		1		2		1			
Left bundle branch block	2					1		1			
Wolff-Parkinson-White	2	1						1			
Other constant intraventricular blocks	5	1				1				3	
Unchanging configuration	3	1				1				1	
Shifting configuration	2									2	
Transient	5	1				1		1		2	

* Intraventricular blocks of all types occur more frequently than expected in men having 10 or more VPC's per 1,000 complexes (p 0.01).

farction.[6] There were 19 men whose standard electrocardiogram showed otherwise unexplained "definite" (0.1 mm.) S–T segment abnormalities or "definite" (flat or inverted) T wave abnormalities of a "nonspecific" nature, or who had a history of chest pain which had been evaluated by the examiner as "probable" or "possible" angina pectoris or coronary insufficiency. These men were categorized as having "probable" coronary heart disease because the evidence did not satisfy the criteria of the Princeton Conference, although it was a reasonable assumption that the abnormalities indicated the presence of coronary heart disease in most, if not all, of these men. Thus, there were 58 men in this random sample of actively employed, ostensibly healthy men who had "definite" or "probable" evidence of coronary heart disease at the time of their first examination (Table IX).

ESTIMATING THE RISK OF CORONARY HEART DISEASE IN THOSE MEN WITHOUT OVERT EVIDENCE OF THE DISEASE AT THE TIME OF THE FIRST EXAMINATION

There were 243 men who were considered to be "at risk," in the sense that they might develop a first event of overt coronary heart disease after the examination. This finding made it worthwhile to attempt to estimate the relative risk for each of the men and to rank them according to this estimated risk. In making this ranking the following "risk factors" were considered:

1. Serum cholesterol level.
2. Evidence of other metabolic abnormalities known to be associated with an enhanced risk of atherosclerosis (such as diabetes mellitus, gout, obesity and xanthelasma).
3. Level of blood pressure.
4. Evidence of complications of hypertensive disease (such as left ventricular hypertrophy on standard electrocardiogram or on x-ray examination).
5. Evidence of arteriosclerosis in other vessels.
6. Presence on the standard electrocardiogram of unexplained abnormalities not directly indicating coronary heart disease (for example, minor S–T and T wave abnormalities and various nonspecific disorders of rhythm or conduction).
7. History of chest pain considered to be "probably not" angina pectoris.

Each of these "risk factors" received a relative weighted "score," and a cumulative score was obtained for each man based on his total number of "risk factors." The procedure that was used is described in detail in a separate publication.[18] When the ranking had been completed, the 58 men with the highest scores (weighted scores greater than 100) were placed in a so-called "high risk" group. In general, these men had hypertension (greater than 160/95 mm. Hg), left ventricular hypertrophy on the electrocardiogram, serum cholesterol levels greater than 300 mg. %, diabetes mellitus, or combinations of these or similar variables. The next 139 men, who had "risk scores" between arbitrary cut-off points of 30 and 100, were placed in a "medium risk" group. In general, these men exhibited such risk factors as a history of gout, a ponderal index lower than 12.000, blood pressure greater than 140/90 mm. Hg or serum cholesterol levels greater than 250 mg. %, or some combination

Table IX. Distribution of Men by Evidence of Coronary Heart Disease and "Risk Factors": Relation to Subsequent Coronary Deaths and Deaths from Other Causes

Coronary Risk Group	Criteria	No. of Men in Group	"Coronary Deaths" No.	"Coronary Deaths" Rate/100	"Deaths, Other Causes" No.	"Deaths, Other Causes" Rate/100
	Men with "definite" and "probable" coronary heart disease					
I	Definite previous myocardial infarction	10	5	50.0	0	0
II	Other definite evidence of coronary heart disease 1. Probable myocardial infarction 2. Acute coronary insufficiency 3. "Typical" angina pectoris 4. Electrocardiographic evidence of old myocardial infarction	29	5	17.2	1	3.4
III	Evidence of probable coronary heart disease 1. Definite S–T segment and T wave abnormalities otherwise unexplained 2. Chest pain, "probably angina pectoris"	19	2	10.5	0	0
	*Men "at risk," with scores weighted according to various "risk factors"**					
IV	"High risk"—weighted score 100 or greater	58	1 (+1)†	1.7 (3.4)	3	5.2
V	"Medium risk"—weighted score 31–99	139	4 (+1)†	2.9 (3.6)	8	5.8
VI	"Low risk"—weighted score 1–30	37	0	0	1	2.7
VII	"Lowest risk"—weighted score 0	9	0	0	0	0
	Total	301	‡17 (+2)†		§13	

* Level of cholesterol; history of diabetes or gout; ponderal index; xanthelasma; level of blood pressure; left ventricular hypertrophy on electrocardiogram or x-ray film; claudication; unexplained "nonspecific" electrocardiographic abnormalities; "nonspecific" chest pain.

† "Possible" coronary deaths.

‡ $\chi^2 = 44.94$; $p = 0.005$; d.f. = 5; (including "possible," $\chi^2 = 43.79$).

§ $\chi^2 = 2.82$, NS; d.f. = 5.

of these or similar factors. Thirty-seven men with weighted scores from 1 to 30 were considered to have a "low risk"; they had only one or two minor "risk factors," such as a ponderal index less than 12.000. There were 9 men in the "lowest" risk group who exhibited none of the risk factors and received scores of zero.

The validity of this ranking has been tested by comparing the distribution of estimated risk at the time of the first examination with the subsequent occurrence of deaths from coronary heart disease (see later). There is a very strong association between these two variables (Table IX). On the other hand, there is no significant association between "coronary risk scores" and subsequent deaths from causes other than coronary heart disease. Although the number of deaths has been small, the findings up to now suggest that the ranking procedure has validity.

RELATION BETWEEN THE PREVALENCE OF CORONARY HEART DISEASE AT THE TIME OF THE FIRST EXAMINATION AND THE PRESENCE OF DYSRHYTHMIAS AND DISORDERS OF CONDUCTION IN THE CARDIAC RECORDINGS

Supraventricular premature contractions and complex supraventricular dysrhythmias were not significantly associated with evidence of coronary heart disease, or with estimated risk of coronary heart disease, at the time of the first examination. These dysrhythmias were essentially as frequent in the "low risk" groups as in those men with overt coronary heart disease (Table x).

Both ventricular premature contractions and complex ventricular dysrhythmias occurred more frequently in the men with coronary heart disease and in those in the "high risk" groups than in the men in the "low risk" groups (Table x). The excess of "observed" over "expected" cases was often as great in the "high risk" group as in the groups with "definite" or "probable" coronary heart disease.

There was no clear association between overt coronary heart disease and the finding of disorders of conduction in the recordings.

SUBSEQUENT DEATHS FROM CORONARY HEART DISEASE AND FROM OTHER CAUSES

Between January 1963, when the examinations began, and January 1969, there were 32 deaths among the 301 men who had been

Table X. Frequency of Dysrhythmias by Coronary Risk Groups I to VII (Based on 283 Complete Recordings)

	Coronary Heart Disease						Men "At Risk"					
	"Definite"				"Probable"		"High Risk"		"Medium Risk"		"Low Risk"	
	I		II		III		IV		V		VI–VII	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
Supraventricular premature contractions (SPC's)												
0/1,000	5	2.4	10	7.0	7	4.6	11	12.7	22	30.7	13	10.6
0.01–0.09/1,000	1	2.7	7	7.8	6	5.1	19	14.2	33	34.4	10	11.8
0.1–0.99/1,000	1	3.6	10	10.6	5	6.9	15	19.3	55	46.6	17	16.0
1–9.9/1,000	1	0.6	1	1.8	...	1.2	4	3.4	11	8.2	1	2.8
>10/1,000	2	0.6	1	1.8	1	1.2	4	3.4	7	8.2	3	2.8
	By analysis of variance, F 1.380, NS											
Bigeminy	1	0.39	1	1.13	...	0.74	3	2.06	4	4.97	2	1.71
Trigeminy	1	0.32	1	0.92	...	0.60	2	1.69	5	4.07	...	1.40
Pairs	2	1.20	4	3.48	2	2.28	8	6.37	16	15.38	2	5.29
Multiple consecutive SPC's	1	0.46	1	1.33	1	0.87	2	2.44	7	5.88	1	2.02
	By χ^2, differences Obs. and Exp. not significant											
Ventricular premature contractions (VPC's)												
0/1,000	3	3.8	10	11.0	4	7.2	15	20.0	49	48.4	26	16.6
0.01–0.09/1,000	...	1.3	4	3.7	4	2.4	5	6.7	20	16.3	3	5.6
0.1–0.99/1,000	2	2.1	5	6.2	6	4.0	13	11.2	23	27.2	11	9.3
1–9.9/1,000	3	1.9	5	5.6	5	3.7	12	10.3	27	24.9	3	8.6
>10/1,000	2	0.9	5	2.5	...	1.7	8	4.7	9	11.3	1	3.9
	By analysis of variance, F 3.292, p 0.01											
Bigeminy	3	0.85	4	2.46	1	1.61	5	4.49	10	10.86	1	3.73
Trigeminy	1	0.60	2	1.74	1	1.14	6	3.19	6	7.69	1	2.64
Pairs	2	1.27	4	3.69	1	2.42	11	6.74	16	16.28	2	5.60
Paroxysmal ventricular tachycardia	...	0.32	1	0.92	...	0.60	5	1.69	3	4.07	...	1.40
VPC's from 3 or 4 foci	2	0.99	5	2.87	1	1.88	7	5.24	12	12.67	1	4.35
	By χ^2, differences Obs. and Exp. not significant except for ventricular bigeminy, which is more frequent in groups I and II (see text).											
Conduction defect												
Sinoatrial block			1				2				1	
Atrioventricular block					1						1	
Intraventricular block	2	0.70	2	2.04	2	1.41	6	3.73	5	9.02	3	3.10
Right bundle branch block	1				1		2		1		1	
Left bundle branch block			1		1							
Wolff-Parkinson-White	1								1			
Other constant intraventricular blocks			1				3				1	
Unchanging configuration			1				1				1	
Shifting configuration							2					
Transient intraventricular blocks							1		3		1	
	By χ^2, differences Obs. and Exp. are not significant											

examined. The immediate cause of 17 of these deaths was very probably coronary heart disease (Table XI). The immediate cause of 2 other deaths may also have been coronary heart disease, but these deaths may well have had other immediate causes, and the evidence is not clear. There were 15 other deaths which were probably not the immediate result of coronary heart disease, although some of those men who died from other causes were known to have coronary heart disease.

Nine of the men who died of coronary heart disease died abruptly and without apparent prodromata. They were observed to be alert and in no apparent distress at one moment and were in the throes of death moments later. One man died suddenly at home one evening while talking to his wife. Two others collapsed on the golf course while their companions watched. Yet another man dived into a swimming pool and failed to emerge; when he was brought to the surface a few minutes later he was apparently dead and could not be revived. Another man was observed to get into his automobile; he started it, drove a few hundred yards, and collapsed. When the witnesses reached him he was apparently dead and could not be revived. Four deaths were not actually observed but were apparently quite abrupt. Two men collapsed while driving automobiles and were found dead. Another, after eating a large meal at a restaurant with a companion, left in apparent good health to go home. Twenty minutes later he was found dead beside his automobile with

the keys in his hand. Yet another man, who had been sleeping in the same bedroom with his wife, arose and went into the bathroom without disturbing her. She was awakened when she heard him fall to the floor. He died within a few moments.

There were eight other deaths which were preceded by pain. Some of these deaths also occurred quite suddenly. Two men were awakened by severe chest pain and died within an hour or less. Two others, who were awake when their precordial distress began, died within less than one-half hour of its onset. Four others had severe chest pain that lasted for several hours or more. Some of these men were seen by a physician, or were admitted to hospitals where the diagnosis of acute myocardial infarction was made. In some instances, the pain had subsided before the death occurred.

Only four of the deaths were fully documented by autopsy as well as by a physician's report and hospital records. Most of the others were documented by a physician's description of the symptoms and signs, the testimony of those who observed the deaths, and, sometimes, hospital records.

It seems quite reasonable to suppose that many, if not all, of the abrupt deaths were caused by a dysrhythmia or by cardiac standstill. These may have been the cause of death in many persons who had the symptoms and signs of acute myocardial infarctions also, even

Table XI. Coronary Deaths: Clinical Characteristics

Code No.	Coronary Risk Group	Findings at Time of First Clinical Examination	Findings on Cardiac Recording*	Circumstances of Death	Source of Data
87	I	Previous myocardial infarction; angina pectoris; ECG: non-specific S–T and T wave abnormalities; cholesterol 268 mg.%; postprandial glycosuria	1.6 SPC's/1,000; 8.2 VPC's/1,000, 4 foci; bigeminy	Died in hospital 3 days after typical acute myocardial infarction. Autopsy, "acute myocardial infarction, massive, anteroseptal"	Hospital records; physician's report, autopsy report
120	I	Previous myocardial infarction; obese; xanthelasma; ECG: Q, V1–V4; right bundle branch block	0.2 VPC's/1,000; 1 focus; right bundle branch block	Awakened with severe chest pain. Died 1 hour under observation at home. Physician's diagnosis, "typical myocardial infarction"	Physician's report; death witnessed
138	I	3 previous myocardial infarctions; angina pectoris; blood pressure 160/95; ECG: pre-excitation syndrome (WPW); S–T and T wave abnormalities; cholesterol 290 mg. %	2.1 VPC's/1,000, 2 foci; constant intraventricular conduction defect (preexcitation syndrome)	At home. Severe precordial pain; marked sweating for 3 hours; then "died abruptly." Physician's diagnosis, "acute myocardial infarction"	Physician's report; death witnessed
141	I	Previous myocardial infarction; probable angina pectoris; possible periods of dysrhythmias; standard ECG: frequent and consecutive APC's and occasional VPC's	92.8 SPC's/1,000; bigeminy; trigeminy; pairs and multiple consecutive SPC's; 16.5 VPC's/1,000, 3 foci; bigeminy, trigeminy, pairs	At home, alert, apparently asymptomatic. Died abruptly in presence of wife.	Physician's report; death witnessed
157	I	Previous myocardial infarction; angina pectoris; blood pressure 140/80 mm. Hg	0.4 SPC's/1,000; aberrantly conducted SPC's; 0.5 VPC's/1,000; 1 focus	Collapsed on golf course; dead when physician arrived 5 minutes later	Physician's report; death witnessed
21	II	Angina pectoris; blood pressure 155/92 mm. Hg; ECG: nonspecific T wave abnormalities; cholesterol 285 mg.%	0.7 SPC's/1,000; 22.4 VPC's/1,000; 3 foci; bigeminy, pairs, ventricular parasystole	Died abruptly in hospital 8 hours after onset of myocardial infarction; documented by history, examination, laboratory and ECG	Hospital records; physician's report; death witnessed
48	II	Previous coronary insufficiency; blood pressure 160/95 mm. Hg; ECG: left bundle branch block, frequent and multifocal VPC's; occasional APC's	17.6 VPC's/1,000; 3 foci; pairs; constant intraventricular block	Subsequent myocardial infarction with recovery; later died abruptly while driving in automobile	Physician's report; death witnessed
328	II	Chest pain: "probably not angina pectoris"; obese; ECG: left bundle branch block	10.4 SPC's/1,000; trigeminy; pairs; aberrantly conducted SPC's; 0.2 VPC's/1,000; 2 foci; intraventricular block (LBBB)	Collapsed while driving an automobile; dead on arrival at hospital	Hospital records; physician's report
332	II	Obese; blood pressure 145/92 mm. Hg; ECG: marked left axis deviation; intraventricular block; "old myocardial infarction"	0.1 SPC's; some aberrant	Died suddenly in hospital 4 hours after onset of acute myocardial infarction documented by signs, symptoms, ECG and laboratory	Hospital records; physician's report; death witnessed
343	II	Typical angina pectoris; blood pressure 170/98 mm. Hg; eyegrounds, KW/Grade III	0 1 SPC's/1,000; multiple SPC's; 17.5 VPC's/1,000, 2 foci; bigeminy; trigeminy	At work, severe chest pain; collapsed. Resuscitation ineffective. Dead on arrival at hospital. Autopsy: "recent posterior septal myocardial infarction; pulmonary edema."	Autopsy report; hospital records; physician's report; death witnessed

Continued

Table XI. Coronary Deaths: Clinical Characteristics (*Continued*)

Code No.	Coronary Risk Group	Findings at Time of First Clinical Examination	Findings on Cardiac Recording*	Circumstances of Death	Source of Data
115	III	Blood pressure 150/95 mm. Hg; ECG: LVH, S–T and T wave abnormalities	3.0 VPC's/1000, 1 focus; shifting A–V block: alternating right and left bundle branch block	Dived into swimming pool and failed to emerge. Resuscitation ineffective. Autopsy: "coronary heart disease."	Physician's report; report of friends; death witnessed
135	III	Blood pressure 170/96 mm. Hg; ECG: LVH; S–T and T wave abnormalities; cholesterol 275 mg. %	0.4 SPC's/1,000; 0.1 VPC's/1,000; 1 focus	Awakened with severe chest pain; died 1 hour. Physician's diagnosis: "typical myocardial infarction"	Physician's report; hospital records; death witnessed
55	IV	Normotensive; no definite evidence of cardiovascular disease; cholesterol 270 mg. %; Standard ECG: "normal" except for few VPC's	Partial recording containing many VPC's; 3 foci; rates not obtainable	Collapsed while driving an automobile; dead on arrival of physician	Physician's report
31	V	Blood pressure 160/90 mm. Hg; Impaired glucose tolerance	0.9 SPC's/1,000; paired SPC's; 1.1 VPC's/1,000; 2 foci	Subsequently had typical angina pectoris; confirmed at re-examination. Collapsed and died suddenly in bathroom with wife nearby. Autopsy: coronary atherosclerosis. No recent infarct.	Autopsy; physician's report; report of wife; death witnessed
101	V	Blood pressure 195/100 mm. Hg; ECG: probable LVH. Chest x-ray: borderline LVH	0.6 SPC's/1,000; possible transient intraventricular conduction defect	Sudden unobserved death within 20 minutes after large meal. Autopsy: pulmonary congestion and LVH; coronary atherosclerosis; no recent infarct.	Physician's report; autopsy report
275	V	History of chest pain; "probably not angina pectoris"; obese; blood pressure 145/90 mm. Hg; ECG: A–V nodal rhythm; minor S–T and T wave abnormalities	44.3 SPC's/1,000; bigeminy; pairs; multiple SPC's; 13.5 VPC's/1,000; 3 foci; bigeminy; pairs; transient intraventricular block	On subsequent exam had atrial fibrillation and many VPC's. Sudden onset of distress at home. Dead on arrival at hospital within 30 minutes. Physician's diagnosis: "acute myocardial infarction"	Physician's report; death witnessed
303	V	Blood pressure 160/104 mm. Hg; cholesterol 276 mg. %	0.08 SPC's/1,000	Collapsed and died on golf course	Physician's report; death witnessed
Two Possible Coronary Deaths					
221	IV	Blood pressure 140/90; ECG: minor S–T and T wave abnormalities; emphysema; chronic alcoholism; impaired glucose tolerance	Partial record 1 SPC/min.	Alleged to have died suddenly of coronary occlusion. No confirming description or observation	Physician's report
334	V	History of hypertension; chest pain, "probably not angina pectoris." Emphysema; chronic bronchitis; blood pressure 150/95; ECG: QRS 0.10; borderline S–T depressions	0.06 SPC's/1,000; 0.03 VPC's/1,000; 1 focus	On re-examination, 1967, chest x-ray showed CT ratio 52% with LVH. Recording shows 10 SPC's/hr. and 10 VPC's/hr.: 3 foci. Impaired glucose tolerance. In bed 1 week at home with cough and dyspnea. Died suddenly in sleep without apparent distress. Death not witnessed	Physician's report

* SPC's and VPC's expressed as rate/1,000.
APC's = atrial premature contractions; CT = cardiothoracic; KW = Keith-Wagner classification; LBBB = left bundle branch block; LVH = left ventricular hypertrophy; SPC = supraventricular premature contraction; VPC = ventricular premature contraction.

though the death occurred during or after the period of pain. The death in the swimming pool may well have been the result of a so-called "diving reflex."[19] The man who died in this way had been re-examined by us approximately one year before his death. At the time of the re-examination he was found to have a constant right bundle branch block and a 2:1 A–V block, which was intermittent. Sometimes during A–V block, his ventricular rate was as slow as 40/min. It seems reasonable to suppose that the vagal effects of the reflex which probably occurred when he dived into the pool may have precipitated complete heart block, and that he died because a spontaneous ventricular rhythm did not take over.

RELATION OF SUBSEQUENT DEATH FROM CORONARY HEART DISEASE TO THE FINDING OF DYSRHYTHMIAS AND CONDUCTION DISTURBANCES AT THE TIME OF THE FIRST EXAMINATION

The number of coronary deaths that occurred among men who had supraventricular premature contractions in their recordings at the time of the first examination was not greater than would be expected on the assumption that all of the men in the sample had the same risk of subsequent death from coronary heart disease (Table XII). The 18 men with 10 or more supraventricular premature contractions/1,000 complexes had 2 more deaths than expected, but this excess is not statistically significant. There were a greater number of deaths than expected among the men who

Table XII. Frequency of Subsequent Coronary Deaths in Men with Certain Dysrhythmias and Conduction Defects (Based on 16 Coronary Deaths in 283 Men with Complete Recordings)

Abnormality	No. of Instances	Coronary Deaths		χ^2	p	Probability of Death	Approx. 95% Confidence Limits
		Obs.	Exp.				
Supraventricular premature contractions							
None	68	4	3.84			0.059	(0.023–0.131)
0.001–0.999/1,000	179	8	10.12	4.30	NS	0.045	(0.038–0.121)
1–9.999/1,000	18	1	1.02			0.056	(0.003–0.263)
>10/1,000	18	3	1.02			0.167	(0.049–0.386)
Complex supraventricular rhythms							
Bigeminy	11	2	0.62	3.37	NS	0.182	(0.033–0.498)
Trigeminy	9	2	0.51	4.78	0.05	0.222	(0.041–0.576)
Paired SPC's	34	4	1.92	2.71	NS	0.118	(0.044–0.254)
Multiple consecutive SPC's	13	3	0.73	7.75	0.01	0.231	(0.069–0.510)
Paroxysmal supraventricular tachycardia	2	0	0.11	0.12	NS	0	(0.000–0.840)
Ventricular premature contractions							
None	107	2	6.05			0.019	(0.003–0.066)
0.001–0.999/1,000	96	5	5.43	12.14	0.01	0.052	(0.023–0.102)
1–9.999/1,000	55	4	3.11			0.073	(0.027–0.174)
>10/1,000	25	5	1.41			0.200	(0.091–0.370)
Complex ventricular rhythms							
Bigeminy	24	5	1.36	8.13	0.005	0.208	(0.080–0.406)
Trigeminy	17	2	0.96	1.26	NS	0.118	(0.022–0.349)
Paired VPC's	36	4	2.06	2.30	NS	0.111	(0.042–0.244)
Paroxysmal ventricular tachycardia	9	0	0.51	0.56	NS	0	(0.000–0.340)
Conduction defects							
Sinoatrial block	4	0	0.23	0.24	NS	0	(0.000–0.600)
Atrioventricular block	2	1	0.11	7.43	0.01	0.500	(0.028–0.972)
Intraventricular block—total instances	20						
RBBB	6	2	0.34	8.80	0.005	0.333	(0.062–0.751)
LBBB	2	2	0.11	15.93	0.005	1.000	(0.214–1.000)
WPW	2	1	0.11	7.43	0.01	0.500	(0.028–0.972)
Other constant intraventricular blocks							
Unchanging configuration	3	1	0.17	4.36	0.05	0.333	(0.018–0.892)
Shifting configuration	2	0	0.11	0.12	NS	0	(0.000–0.840)
Transient intraventricular blocks	5	1	0.28	1.96	NS	0.200	(0.011–0.510)
Intraventricular blocks, total men	19	6	1.07	25.66	0.005	0.316	(0.165–0.513)

Exp. = expected; LBBB = left bundle branch block; NS = not significant; Obs. = observed; RBBB = right bundle branch block; SPC's = supraventricular premature contractions; VPC's = ventricular premature contractions; WPW = Wolff-Parkinson-White syndrome.

exhibited each of the complex supraventricular dysrhythmias except paroxysmal supraventricular tachycardia, and this excess was statistically significant in the case of supraventricular trigeminy and multiple consecutive supraventricular premature contractions. However, many of the men who exhibited these dysrhythmias also had other electrocardiographic abnormalities, as well as evidence of other nonelectrocardiographic "risk factors," and it cannot be assumed that the excess of observed deaths is necessarily attributable to these specific dysrhythmias.

The number of coronary deaths that occurred among men who had ventricular premature contractions in their recordings was significantly greater than expected on the assumption of an equal risk of subsequent death from coronary heart disease for all men in the sample (Table XII). This was especially true of the men who had 10 or more ventricular premature contractions/1,000 complexes in their initial recordings. The apparent probability of death for such men was 10 times greater than that of men with no ventricular premature contractions in their original recordings. Statistically, this is highly significant (p 0.005). The occurrence of complex ventricular rhythms was also associated with a greater number of deaths than expected, and in the case of ventricular bigeminy this excess was statistically significant. Both of these observations are consistent with the preceding data, thus indicating that there is a close association between ventricular dysrhythmias and other nonelectrocardio-

graphic factors which increase the risk of death from coronary heart disease. Although the risk associated with ventricular premature contractions in the recording may merely reflect the added risk that accompanied the other risk factors with which ventricular premature contractions are associated, this does not seem to be the case (see the following).

Much of the apparent increase in risk associated with ventricular bigeminy may be related to the association between this rhythm and large numbers of ventricular premature contractions. It is not clear whether bigeminal and trigeminal rhythms in themselves carry any added risk over and above that associated with many ventricular premature contractions. On the other hand, paired ventricular premature contractions and brief periods of paroxysmal ventricular tachycardia apparently were not associated with any greater risk than that indicated by the presence of ventricular premature contractions in the recording. Nine men in the sample had one or more periods of paroxysmal ventricular tachycardia during their initial recordings, and none of these men died during the subsequent five years.

Disturbances of atrioventricular conduction and disturbances of intraventricular conduction also appear to be associated with an enhanced risk of death from coronary heart disease (Table XII). This risk appears to be about the same as that associated with the presence of many ventricular premature contractions, but the same considerations apply to it that apply to the risk associated with ventricular dysrhythmias. Intraventricular block and similar conduction defects are usually detectable on the standard electrocardiogram and are known to be closely associated with coronary heart disease. The risk associated with such conduction defects may largely reflect the risk that is associated with pre-existing coronary heart disease, which is detectable by other means. It is not clear whether conduction defects make an independent contribution to risk. However, the fact that one third of all men who had conduction defects died within the next five years suggests that these defects carry with them a distinct added risk.

Men with no dysrhythmias and no conduction defects and those with only a single dysrhythmia consisting of supraventricular or ventricular premature beats had fewer subsequent deaths than expected (Table XIII). Those with complex dysrhythmias as well as premature contractions had approximately as many deaths as expected, but men with more than 10 supraventricular premature contractions/1,000 and also more than 10 ventricular premature contractions/1,000 had more deaths than expected (p 0.01).

Men with combinations of supraventricular dysrhythmias and conduction defects had no more deaths than expected, but men with ventricular dysrhythmias and conduction defects and those with both supraventricular and ventricular dysrhythmias as well as conduction defects had significantly more deaths than expected (Table XIII). The indicated probabilities of death of men in the last two categories were 57 and 22 per cent, respectively, in the subsequent five years.

The coronary risk groups into which the men in the sample were divided reflected many of the major "risk factors" that are known to influence the likelihood of death from coronary heart disease. Therefore, these risk groups were utilized in an attempt to determine if the occurrence of asymptomatic dysrhythmias and conduction defects in the recordings made a contribution to the risk of death which was independent of that contributed by other risk factors (Table XIV). The hypothesis was established that, if this were true, men with a given dysrhythmia or conduction defect would have a greater number of subsequent deaths from coronary heart disease than other men in the same risk group. In making these comparisons, groups VI and VII (the "lowest" risk groups) could not be utilized, since no coronary deaths had occurred in these groups; group IV (the "high risk" group) could be utilized only if the men with partial recordings were considered as well as the men with complete recordings, because the only coronary death occurred in a man with a partial recording. Within these limitations the data indicate that supraventricular dysrhythmias made no contribution to risk of death, but that ventricular dysrhythmias were associated with a greater than expected number of deaths in each category. This suggests that ventricular dysrhythmias may have made a significant independent contribution to the risk of death from coronary heart disease; but the data available up to now are not sufficient to provide a firm indication of whether or not this is actually the case.

Discussion

The findings suggest that asymptomatic dysrhythmias and disorders of cardiac conduction are exceedingly common in American men in their mid-50's. Three quarters of the 301

Table XIII. Frequency of Subsequent Coronary Deaths in Relation to Certain Combinations of Dysrhythmias and Conduction Defects (Based on 16 Coronary Deaths in 283 Men with Complete Recordings)

	No. of Instances	Coronary Deaths		χ^2	p	Probability of Death	Approx. 95% Confidence Limits
		Obs.	Exp.				
All complete recordings	283	16	...	...	...	0.0565	
1. No SPC's, VPC's, conduction defects	22	0	1.24	1.43	NS	0	(0.000–0.160)
2. No complex dysrhythmias and no conduction defects							
a. SPC's only	66	2	3.73	1.11	NS	0.030	(0.006–0.105)
<1 SPC/1,000 complexes	59	2	3.34	0.72	NS	0.034	(0.006–0.114)
b. VPC's only	21	0	1.19	1.36	NS	0	(0.000–0.160)
<1 VPC/1,000 complexes	16	0	0.90	1.02	NS	0	(0.000–0.210)
c. SPC's and VPC's only	69	3	3.90	0.29	NS	0.043	(0.021–0.112)
3. Conduction defects only							
a. Definite conduction defects	4	0	0.23	0.24	NS	0	(0.000–0.600)
b. Possible transient intraventricular conduction defects	1	0	0.06	0.06	NS	0	(0.000–0.980)
4. PC's and complex dysrhythmias only (no conduction defects)							
a. Supraventricular dysrhythmias	77	2	4.35	1.85	NS	0.026	(0.004–0.090)
b. Ventricular dysrhythmias	35	0	1.98	2.39	NS	0	(0.000–0.100)
c. Supraventricular and ventricular dysrhythmias	125	8	7.07	0.23	NS	0.064	(0.040–0.092)
>10 SPC's/1000 and >10 VPC's/100	2	1	0.11	7.43	0.01	0.500	(0.028–0.972)
5. PC's, complex dysrhythmias and conduction defects							
a. Supraventricular dysrhythmias and conduction defects	4	0	0.23	0.24	NS	0	(0.000–0.600)
b. Ventricular dysrhythmias and conduction defects	7	4	0.40	35.67	0.005	0.571	(0.232–0.857)
c. Supraventricular and ventricular dysrhythmias and conduction defects	9	2	0.51	4.78	0.05	0.222	(0.041–0.576)

Exp. = expected; Obs. = observed; PC's = premature contractions; SPC's = supraventricular premature contractions; VPC's = ventricular premature contractions.

members of this sample of steadily employed active men had supraventricular premature contractions during the course of a six-hour recording period, approximately two thirds had ventricular premature contractions, and one man in 20 had a disturbance of conduction. Furthermore, 6.4 per cent of these men had 10 or more supraventricular premature contractions/1,000 complexes and 17.7 per cent of them had complex supraventricular dysrhythmias during the course of the recording; 8.8 per cent had 10 or more ventricular premature contractions/1,000 complexes, and 19.1 per cent had complex ventricular dysrhythmias; 7.7 per cent had disturbances of intraventricular conduction. So far as one could ascertain from observing them and talking to them during the periods in which the recordings were made, all of them were essentially unaware of the occurrence of these episodes of disturbed cardiac function.

The evidence is consistent with a hypothesis that ventricular premature contractions, other ventricular dysrhythmias and intraventricular conduction defects are manifestations of underlying coronary heart disease. These phenomena are distributed within the sample in parallel with the evidence of coronary heart disease and in parallel with the evidence of increased risk of coronary heart disease; and their presence was associated with an increased risk of subsequent death from coronary heart disease.

Supraventricular dysrhythmias were not distributed in this manner and do not appear to be manifestations of underlying coronary heart disease, although the evidence suggests that the frequency of their occurrence may be influenced by the presence of manifestations of coronary heart disease. Men who have very frequent supraventricular premature contractions and complex supraventricular dysrhythmias appear

Table XIV. Frequency of Subsequent Coronary Deaths in Men with Dysrhythmias and Conduction Defects by Coronary Risk Groups I to V (Based on 16 Coronary Deaths in 283 Men with Complete Recordings)

	Definite and Probable Coronary Heart Disease (Risk Groups I–III)		Men "At Risk" "High Risk" (Risk Group IV)		"Medium Risk" (Risk Group V)		Cumulative χ^2
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	
Supraventricular premature contractions							
None	4	4.55	...	..	...	0.69	
Any	8	7.45	...	...	4	3.31	
χ^2; p		1.47; NS	...	...	...	0.86; NS	2.33; NS
(d.f.)		(1)				(1)	(2)
<10/1,000	10	11.17	...	...	3	3.78	
≥10/1,000	2	0.83	...	...	1	0.22	
χ^2; p		2.25; NS				2.04; NS	4.29; NS
(d.f.)		(1)				(1)	(2)
Ventricular premature contractions							
None	1	3.52	...	0.28	1	1.53	
Any	11	8.48	1	0.72	3	2.47	
χ^2; p		3.21; NS		0.39; NS		0.31; NS	3.91; NS
(d.f.)		(1)		(1)		(1)	(3)
<10/1,000	8	10.55	...	0.83	3	3.34	
≥10/1,000	4	1.45	1*	0.17	1	0.66	
χ^2; p		6.45; 0.025		5.09; 0.025		2.04; NS	13.58; 0.005
(d.f.)		(1)		(1)		(1)	(3)
Intraventricular conduction defects							
None	7	10.97	...	...	3	3.84	
Any	5	1.03	...	...	1	0.16	
χ^2; p		20.97; 0.005				4.89; 0.05	25.86; 0.005
(d.f.)		(1)				(1)	(2)

* Without this man, the cumulative χ^2 is 8.49, p 0.025 (see text).

to have a somewhat increased risk of subsequent death from coronary heart disease; but this may well be the result of the statistical association between such frequent and complex supraventricular dysrhythmias and the occurrence of ventricular dysrhythmias and other manifestations of coronary heart disease.

Whether or not a man had evidence of overt coronary heart disease at the time of the first examination, the presence of ventricular premature contractions and intraventricular conduction defects in his recording was associated with an increased likelihood of his subsequently dying from coronary heart disease. The evidence suggests that ventricular dysrhythmias and conduction defects made an independent contribution to risk of death from coronary heart disease over and above the contribution to risk from all the other risk factors with which they were associated. Further observations will be necessary before firm conclusions can be drawn.

Although the presence of asymptomatic ventricular dysrhythmias and intraventricular conduction defects indicated an increased risk of death from coronary heart disease in these middle-aged men, the immediate prognostic significance of these electrocardiographic phenomena is not so dire as one might have expected from the startling nature of some of the dysrhythmias that were discovered. Many men who had periods of ventricular bigeminy and trigeminy, paired beats, paroxysmal ventricular tachycardia and transient intraventricular block have lived asymptomatically and in apparent health for five or more years since these episodes were discovered. The occurrence of one or more episodes of paroxysmal ventricular tachycardia in single six-hour recordings of nine men (3 per cent of the sample) suggests that thousands of such episodes must have occurred in these men since that time, and that in all instances the heart reverted promptly to an effective rhythm and pattern of conduction. One who observes these recordings is not so much surprised by the fact that many of these men later died suddenly, as by the fact that so many of them remained alive and apparently well during the next five years. Nevertheless, the clinical characteristics of the ultimate death of those who did die of

coronary heart disease suggest quite strongly that a dysrhythmia or cardiac standstill was the immediate cause of many of these deaths. This suggests that the finding of dysrhythmias and conduction disturbances in the six-hour record of a middle-aged man indicates that the subject has a susceptibility to dysrhythmia and to dysrhythmic death, which is greater than that of other men whose tracings are free from these phenomena.

The supraventricular dysrhythmias seen in these men evidently arose from some process different from that which produced the ventricular dysrhythmias. The two types of dysrhythmia were not closely associated with each other. The occurrence of supraventricular dysrhythmias was not closely associated with evidence of coronary heart disease at the time of the examination, and their occurrence alone in the absence of other dysrhythmias or conduction defects was not associated with any significantly enhanced risk of subsequent death from coronary heart disease. Evidence from other aspects of these studies suggests that the supraventricular dysrhythmias seen in these men were in part associated with the presence of pulmonary disease. This will be the subject of further study.

Taken as a whole, the findings from these investigations suggest that the occurrence of transient ventricular dysrhythmias and conduction disturbances in middle-aged American men is an indication of underlying coronary heart disease and of an increased risk of dying because of this disease. For these reasons it appears that the procedure of obtaining large samples of electrocardiographic complexes under the conditions of ordinary activity and analyzing these for dysrhythmias and conduction defects may be a useful diagnostic tool in the clinical study of coronary heart disease, and that this procedure may provide another useful indicator of the presence of this disease in the subjects of epidemiologic studies.

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